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Fish & Neave  
1251 Avenue of the Americas  
New York, NY 10020

EXAMINER

LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/706,128	<b>Applicant(s)</b> XIE ET AL.	
	<b>Examiner</b> Cheyne D. Ly	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-17 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) 1-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16,17 and 19-21 is/are rejected.
- 7) ☒ Claim(s) 16 is/are objected to.
- 8) ☒ Claim(s) 1-17 and 19-21 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>8/10/04</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicants' arguments filed February 11, 2005 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. The withdrawal of claims 1-15, cancellation of claim 18, and addition of claims 19-21 have been acknowledged.
3. The new title has been accepted.
4. Applicant's argument directed to the Sequence Compliance issue has been found to be persuasive because the statement is present the Statement in Support of Amendment to Sequence Listing, filed September 18, 2003.
5. Claims 16, 17, and 19-21 are examined on the merits.

### **OBJECTIONS**

6. Claim 16 is objected to because, as amended, said claim ends with a semicolon from line 16, and a period from line 20. Appropriate correction is required. Applicant has been advised to remove the semicolon from line 16.

### **CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH**

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 16, 17, and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
9. The instant rejection has been necessitated by claim amendments.
10. Claim 16, line 5, recites the limitation of “wherein all or part of the atomic coordinates...are determined to comprise a binding pocket...” which causes said claim to be vague and indefinite. It is noted that the limitation of “part of the atomic coordinates...” has been reasonably construed as comprising one amino acid. Further, Applicant has disclosed (page 9) a binding pocket defined by a plurality of amino acids. Therefore, it is not clear whether “a binding pocket” is determined by one amino acid, or a plurality of amino acids. Claims 17, 19, and 20 are rejected for being dependent from claim 16.
11. Claim 20, line 2, recites “prior to step a)” which causes said claim to be vague and indefinite because claim 16 or 17 from which claim 20 depends does not recite “step a).”
12. Claim 20, lines 3-4, recites the limitation of “JNK3...or JNK3 mutant molecule and a chemical entity” causes said claim to be vague and indefinite because it is not clear whether the limitation of “chemical entity” is associated with only the JNK3 mutant. Or

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the “chemical entity” is also associated with JNK3. The same issue is present in claim 21, lines 3-4. Clarification of the metes and bounds is required.

13. Claim 20, lines 5-7, recites “said JNK3 or JNK3 mutant molecule” having the specified N-terminal deletion and C-terminal deletion. However, it is not clear whether only the recited JNK3 mutant molecule has the deletions. Or does JNK3 also have the deletions. The same is present in claim 21, lines 5-7. Clarification of the metes and bounds is required.

#### **REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

#### **NEW MATTER**

15. The instant rejection has been necessitated by claim amendments.
16. Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. Claim 20, i), and claim 21, a), recite the limitation of “an N-terminal deletion of about 40 amino acids and a C-terminal deletion of about 20 amino acids” which has not been found in the instant specification. It is noted that Applicant discloses crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and utilize the atomic coordinates generated from said crystals (Examples 1-6). However, said disclosure does not provide written description basis for the new limitation in claims 20 and 21.

#### LACK OF ENABLEMENT

18. Claims 16, 17, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure and generating atomic coordinates of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, does not reasonably provide enablement for any JNK3 or JNK3 mutant molecule. Further, the instant specification does not provide enablement for methods that rely on atomic coordinates from any JNK3 or any JNK3 mutant molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

19. The instant rejection has been necessitated by claim amendments.

20. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

21. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and utilize the atomic coordinates generated from said crystals (Examples 1-6).

22. However, a method that relies on data from an unpredictable art such as protein crystallization would require clear and precise guidance for one skilled in the art to reliably use the said method. It is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a New Focus article

depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essence, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). As discussed below, the specification does not provide adequate disclosure to enable the claimed invention.

23. For example, claims 16, 17, and 19-21 are directed to atomic coordinates from any JNK3 which has been reasonably construed to comprise the wild-type JNK3. However, the instant specification provides enablement disclosure for making crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Example 2). Therefore, the instant specification does not provide enablement support for claims 16, 17, and 19-21 as directed to atomic coordinates from any JNK3. It is noted that said claims recite the limitation of "according to Figure 1A." However, said figure "lists the atomic structure coordinates for unphosphorylated JNK3" (page 5, line 3). Therefore, said Figure 1A does not specifically support for any JNK3 molecule beyond the disclosed unphosphorylated JNK3.

24. For example, claims 16, 17, and 19 are directed to any JNK3 mutant molecule. Claims 20 and 21 are directed "an N-terminal deletion of about 40 amino acids and a C-terminal



deletion of about 20 amino acids.” However, the instant specification provides enablement disclosure for making crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Examples 1-6). Therefore, the instant specification does not provide enablement support for claims 16, 17, and 19-21 as directed to any JNK3 mutant molecule, or one with “an N-terminal deletion of about 40 amino acids and a C-terminal deletion of about 20 amino acids.” It is noted that said claims recite the limitation of “according to Figure 1A.” However, said figure “lists the atomic structure coordinates for unphosphorylated JNK3” (page 5, line 3). Therefore, said Figure 1A does not specifically support for any JNK3 mutant molecule beyond the disclosed unphosphorylated JNK3.

25. For example, claims 20 and 21 are directed to “producing a crystal of a JNK3.”

However, the instant specification provides enablement disclosure for making crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Examples 1-6). Therefore, the instant specification does not provide enablement support for claims 20 and 21 as directed to any JNK3 molecule beyond the disclosed JNK3 crystal.

26. Accordingly, it would be unpredictable for one skilled in the art to make crystal structures of other molecules beyond the ones of the instant case where specific coordinates are disclosed. In light of the difficulty of the protein crystallization process,

it is, therefore, unreasonable to expect one skilled in the art to use the information disclosed for specific crystals to make other of predictable quality to practice the method of the claimed invention without undue experimentation.

## **RESPONSE TO ARGUMENTS**

27. Applicant argues that the instant rejection has overcome by the claim amendments.

Applicant's argument is not persuasive because said amendments have necessitate the instant rejection as discussed above.

28. Applicant points to the specification to argue that the "specification enables the full scope of the amended claims." Applicant's argument and pointed to support have been acknowledged. However, as discussed above, the instant specification provides enablement disclosure for making crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Examples 1-6). Therefore, the instant specification does not provide enablement support for the full scope of claims 16, 17, and 19-21.

29. Applicant argues that Su et al. "teaches how to make and purify several JNK3 mutants."

Applicant's argument is not persuasive because the disclosure Su et al. is directed to the specific mutation of changing the "methionine residue to an alanine" (Su et al., column 9, lines 39-43). As discussed above, in light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to use the

information disclosed for a specific crystal to make other of predictable quality to practice the method of the claimed invention without undue experimentation.

30. Applicant argues that Scapin et al. provides as Exhibit B provides enablement support for the claimed invention. It is noted the Exhibit B is not present in the instant Application. Further, Scapin et al. is not present in the IDS, filed August 10, 2004, or February 26, 2001. Therefore, Applicant's argument is not persuasive because the argue Exhibit B is available for consideration.

31. Claims 16, 17, and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Examples 1-6), does not reasonably provide enablement for a method for identifying both an agonist and an antagonist of a molecule comprising a binding pocket in the JNK3 molecule or JNK3 mutant molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

32. It is acknowledged that Applicant has disclosed information to enable one skilled in the art to make crystal structures of JNK3 without the first 39 residues, and JNK3 lacking the N-terminal 39 and C-terminal 20 residues, and generating atomic coordinates from said crystals (Examples 1-6) for practicing the claimed invention as directed to the

identification of inhibitors Examples 5 and 6. However, the instant specification does not enable one of skill in the art to practice the claimed invention as directed to identifying both an agonist and an antagonist of a molecule comprising a binding pocket in the JNK3 molecule or JNK3 mutant molecule with the same binding pocket atomic coordinates. For example, different effectors, agonists or antagonists, have different functions, which are defined by their respective chemical and biochemical properties. These distinct chemical and biochemical properties determine how either agonists or antagonists interact with JNK3, therefore, determine their respective mechanisms of action. How are such different effectors with distinct chemical and biochemical properties identified by the same method such as the one in Examples 5 and 6? The lack of guidance provided by the instant specification as to how one of skill in the art to use the claimed method as directed to the identification of either an agonist or antagonist causes to be not enabled commensurate in scope with these claims. Therefore, one skilled in the art would require undue experimentation to predictably practice the claimed invention.

## **RESPONSE TO ARGUMENTS**

33. Applicant argues that claims 16 and 17 are enabled as amended. Applicant's argument has been found to be unpersuasive because the claim amendments have not overcome the instant rejection as discussed above. Applicant further argues that "the amendment refers to JNK3 mutant molecules that are within 1.5 Å rms deviation with respect to the wild-type JNK3 molecule described in Fig. 1A." Applicant's argument is not persuasive because the recitation rms deviation does not support how different effectors with distinct chemical and biochemical properties identified by the same method such as the one in

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Examples 5 and 6? It is noted that claims 16 and 17 do not recite any wild-type limitation.

### **CLAIM REJECTIONS - 35 USC § 103**

34. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

35. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

36. Claims 16, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Su et al. (US 6,162,613 A) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983).

37. The instant rejection has been necessitated by claim amendments.

## **RESPONSE TO ARGUMENTS**

38. Applicant argues that the claims have been amended which “reflects a step whereby the practitioner determines that all or part of a set of amino acids constitutes a JNK3 or JNK3 mutant molecule binding pocket of interest for designing or selecting a potential agonist or antagonist.” It is noted that the limitation of “wherein all or part of the atomic coordinates...” is directed to nonfunctional descriptive material, which does not distinguish the invention from the prior art in term of patentability. Therefore, as cited below, the claimed invention as amended is obvious in view of Su et al. and In re Gulack.

39. Specific to the argument of “the determination step...”, the method of Su et al. is based upon the identification of residues in the ATP-binding pocket of a first kinase that make close contacts with an inhibitor (column 3, lines 24-29). Therefore, as cited below, the claimed invention as amended is obvious in view of Su et al. and In re Gulack.

## **BASIS FOR REJECTION**

40. Su et al. discloses a method for identifying an inhibitor (agonist or antagonist) of JNK3 (claim 6). The method of Su et al. comprises using X-ray coordinates, contact between JNK3 and inhibitors are determined via modeling and binding assays, and inhibitors such as pyridinyl-imidazoles (SB203580) are identified according interactions with the binding pocket (Examples 4 and 5) wherein the inhibitor is created (column 4, lines 16-20). The method of Su et al. is based upon the identification of residues in the ATP-

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binding pocket of a first kinase that make close contacts with an inhibitor (column 3, lines 24-29), as in instant claims 16, 17, and 19.

41. Even though the method disclosed by Su et al. does not specify that the atomic coordinates of JNK3 according to Figure 1, the specific limitations of atomic coordinates in this instant case do not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.
42. In re Gulack defines nonfunctional descriptive material, as when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in term of patentability. Also, the MPEP indicates that descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition (MPEP § 2106 (IV)(B)(b)). Specific to the instant case, atomic coordinates in Figure 1A are merely stored so as to be read or outputted by a computer without creating any functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer, then such descriptive material alone does not impart functionality either to the data as so structured, or to the computer.
43. Clearly, an artisan of ordinary skill in the art would have been motivated to partake the method emphasized by Su et al. to practice the said for identifying inhibitors of JNK3.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Su et al. for identifying inhibitors of JNK3.

### CONCLUSION

44. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
45. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.
46. This application contains claims 1-15 drawn to an invention nonelected, filed September 18, 2003. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.



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47. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. The USPTO's official fax number is (571) 273-8300.
48. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.
49. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.
50. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

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51. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

C. Dune Ly / *CDL*

5/12/05

*Ardin H. Marschel 5/15/05*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER